

Figure 1

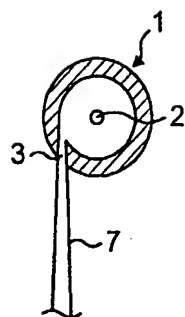


FIG. 2

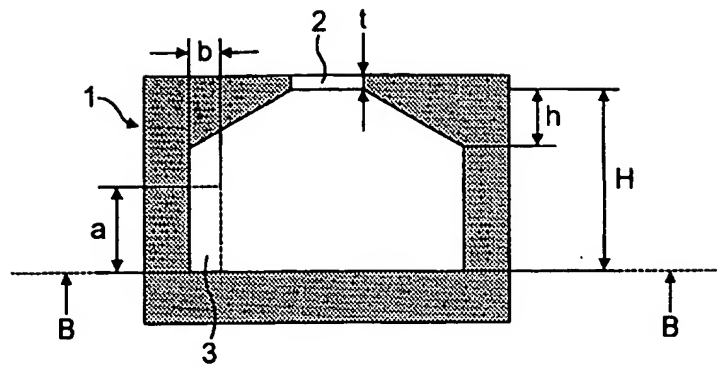


FIG. 3

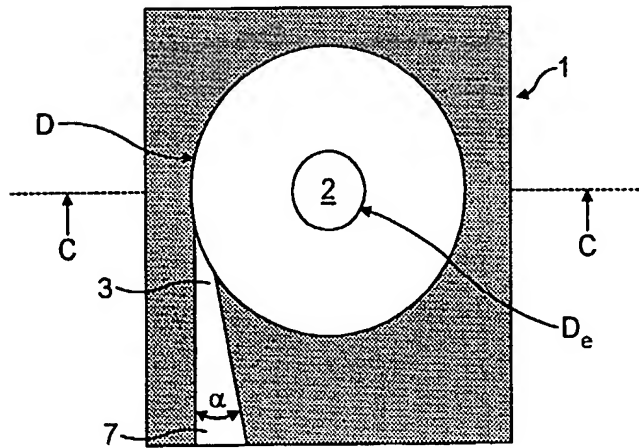


FIG. 4

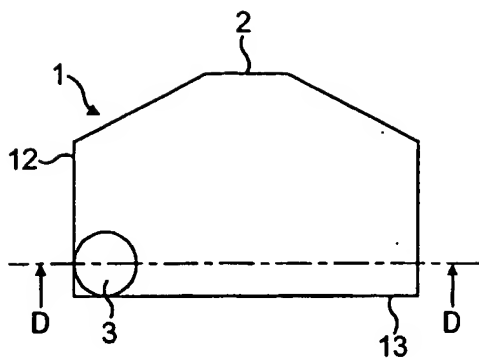


Figure 5a

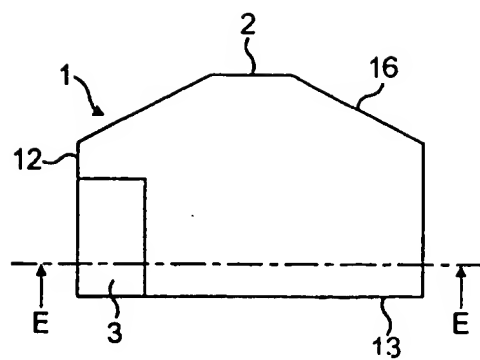


Figure 6a

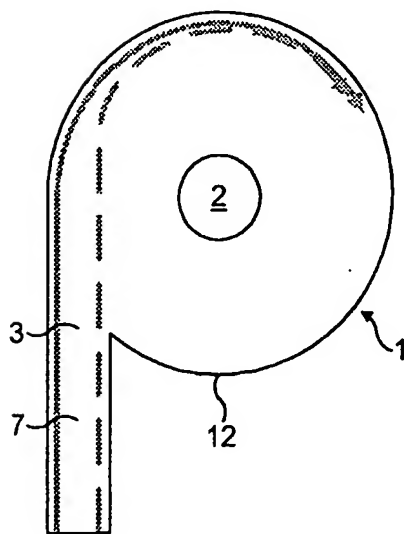


Figure 5b

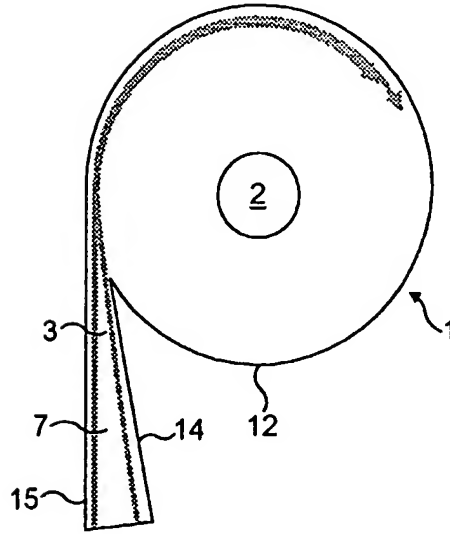


Figure 6b

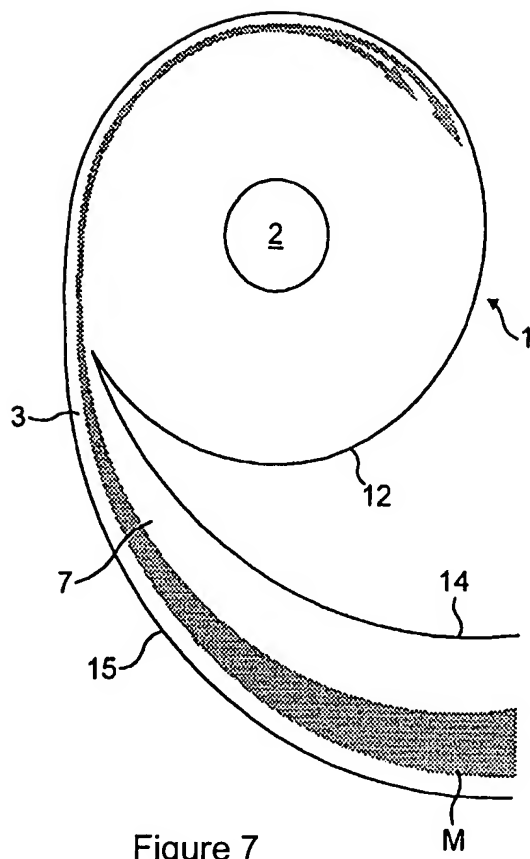


Figure 7

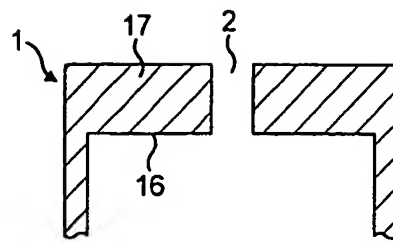


Figure 8

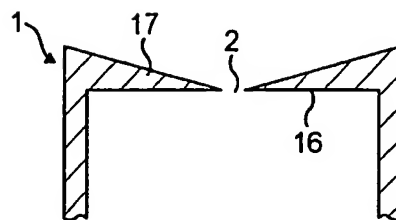


Figure 9

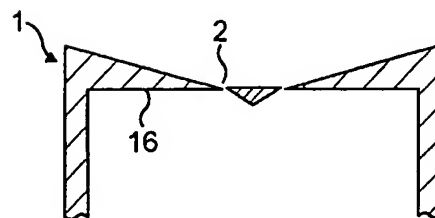


Figure 10

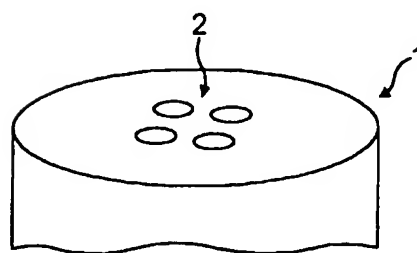


Figure 11

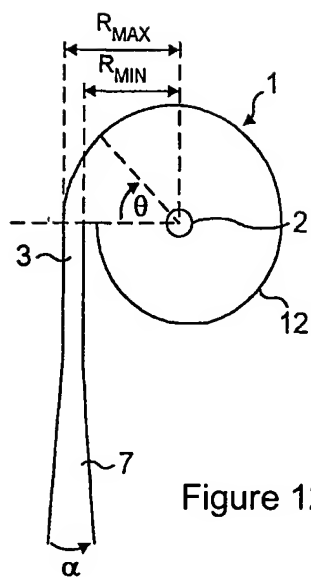


Figure 12

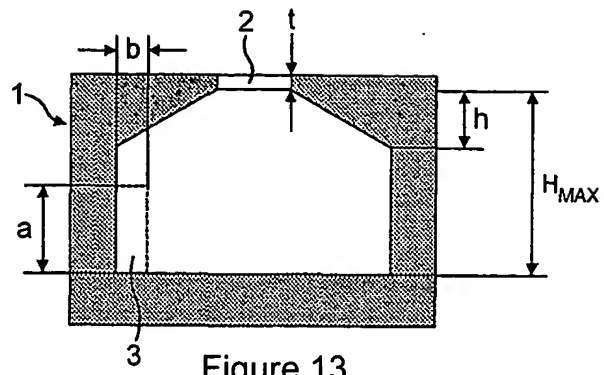


Figure 13

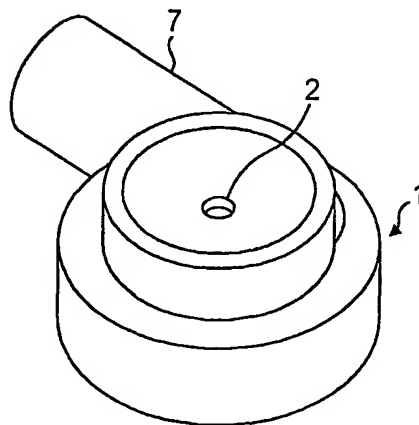


Figure 14

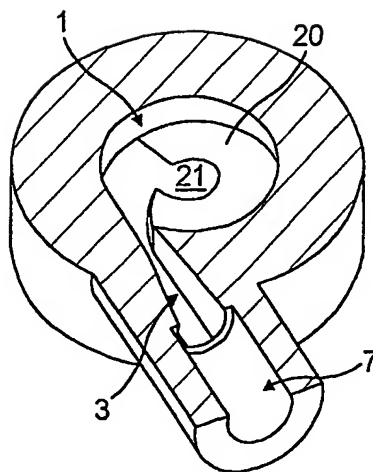


Figure 15

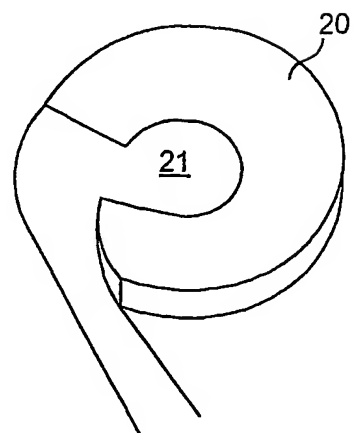


Figure 16

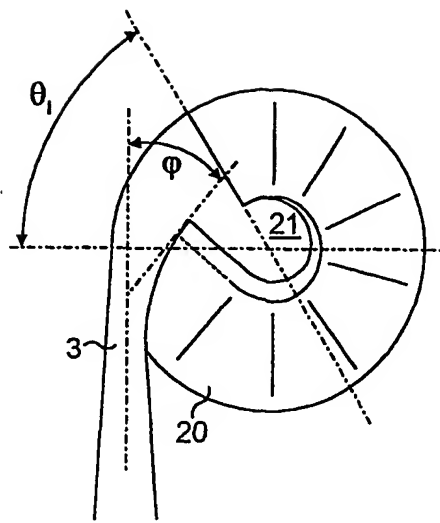


Figure 17

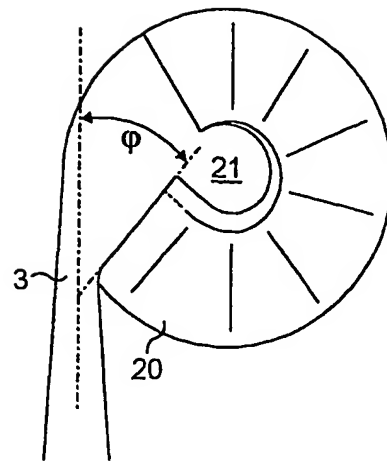


Figure 18

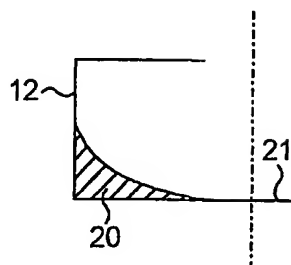


Figure 19

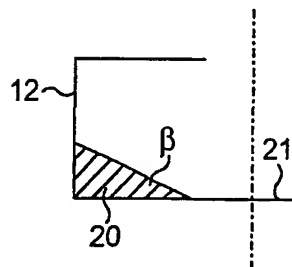


Figure 20

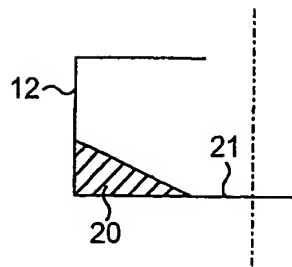


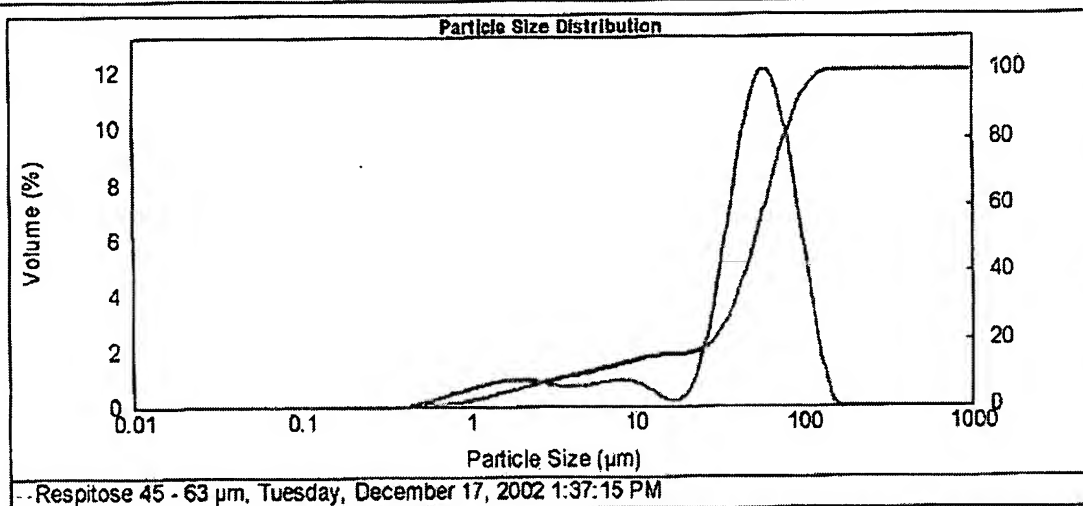
Figure 21

Result Analysis Report

Sample Name:
Respitose 45 - 63 µm

Particle Name: Lactose	Accessory Name: Hydro 2000SM (A)	Obscuration: 10.11 %
Particle RI: 1.347 Absorption: 0.1	Analysis model: General purpose	Obscuration (blue): 6.69 %
Dispersant: Cyclohexane	Dispersant RI: 1.426	Weighted Residual: 0.922 %

Vol. Weighted Mean D[4,3]: 53.494 µm	Mode: 59.194 µm	Specific Surface Area: 0.504 m ² /g
Surface Weighted Mean D[3,2]: 11.916 µm	Span: 1.676	Concentration: 0.0247 %Vol
Result units: Volume Uniformity: 0.462		
d(0.1): 5.203 µm	d(0.5): 52.769 µm	D(0.60): 59.94 µm
		d(0.9): 93.671 µm



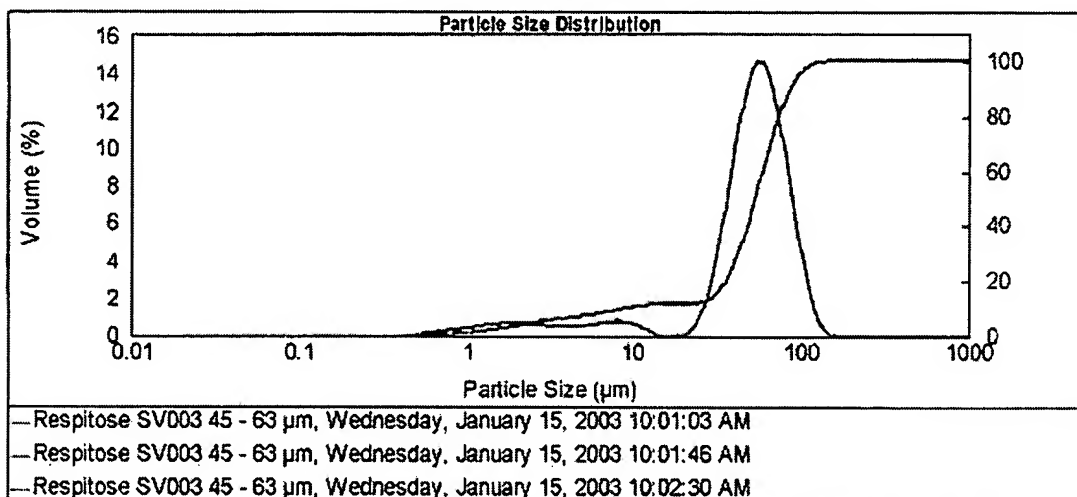
Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %
0.010	0.00	0.105	0.00	1.055	1.88	11.482	14.27	120.226	98.02	1259.825	100.00
0.011	0.00	0.120	0.00	1.259	2.52	13.183	14.76	136.033	99.89	1445.440	100.00
0.013	0.00	0.136	0.00	1.445	3.23	15.135	15.05	158.469	100.00	1656.587	100.00
0.015	0.00	0.153	0.00	1.660	4.02	17.378	15.19	181.970	100.00	1905.481	100.00
0.017	0.00	0.182	0.00	1.905	4.84	19.863	15.37	200.500	100.00	2187.782	100.00
0.020	0.00	0.209	0.00	2.188	5.67	22.609	15.53	229.883	100.00	2511.895	100.00
0.023	0.00	0.240	0.00	2.512	6.49	25.303	17.32	275.423	100.00	2884.032	100.00
0.030	0.00	0.275	0.00	2.894	7.74	30.200	20.04	318.228	100.00	3311.311	100.00
0.035	0.00	0.315	0.00	3.311	7.83	34.574	24.54	363.078	100.00	3801.604	100.00
0.035	0.00	0.363	0.00	3.802	8.57	39.811	31.07	416.889	100.00	4365.159	100.00
0.040	0.00	0.417	0.00	4.365	9.19	45.709	39.55	479.630	100.00	5011.872	100.00
0.046	0.00	0.479	0.00	5.012	9.82	52.481	43.58	549.541	100.00	5754.395	100.00
0.052	0.00	0.556	0.00	5.754	10.49	60.216	60.42	630.957	100.00	6606.934	100.00
0.060	0.00	0.631	0.25	6.607	11.22	69.183	71.13	724.436	100.00	7525.176	100.00
0.067	0.00	0.726	0.53	7.595	12.01	79.423	80.81	831.764	100.00	8705.638	100.00
0.079	0.00	0.832	0.89	8.710	12.82	91.201	88.71	954.683	100.00	10000.000	100.00
0.091	0.00	0.955	1.34	10.000	13.00	104.713	94.47	1096.478	100.00		

Figure 22(a)

R sult Analysis Report

Sample Name:
Respitose SV003 45 - 63 µm

Particle Name: Lactose	Accessory Name: Hydro 2000SM (A)	Obscuration: 12.22 %
Particle RI: 1.347 Absorption: 0.1	Analysis model: General purpose	Obscuration (blue): 7.33 %
Dispersant: Cyclohexane	Dispersant RI: 1.426	Weighted Residual: 0.627 %
Vol. Weighted Mean D[4,3]: 53.816 µm	Mode: 57.308 µm	Specific Surface Area: 0.41 m ² /g
Surface Weighted Mean D[3,2]: 14.626 µm	Span: 1.464	Concentration: 0.0361 %Vol
Result units: Volume	Uniformity: 0.384	
d(0.1): 6.571 µm	d(0.5): 53.682 µm	D(0.60): 59.54 µm
		d(0.9): 67.148 µm

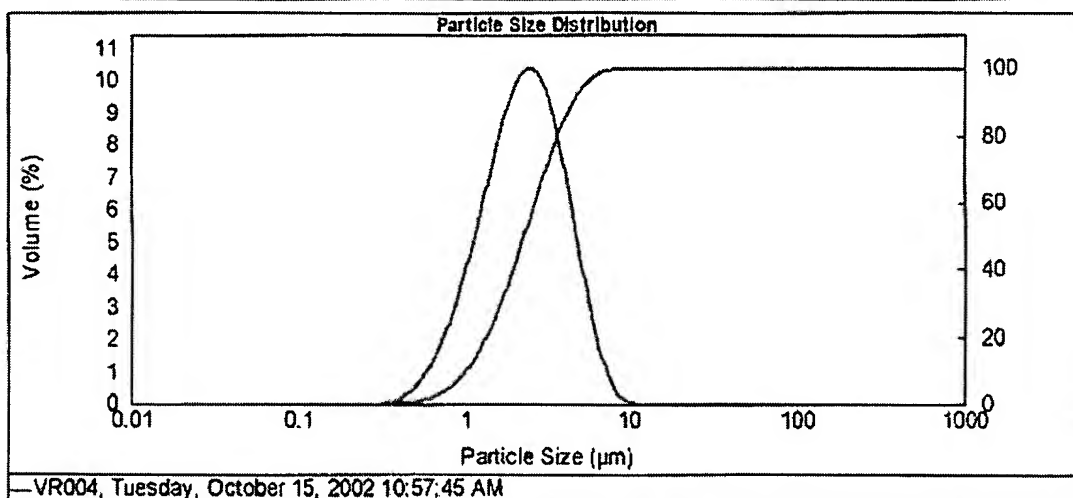


Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %	Size (µm)	Vol Under %
0.010	0.00	0.105	0.00	1.056	1.40	11.402	11.77	120.225	99.21	1258.925	100.00
0.011	0.00	0.120	0.00	1.250	1.68	13.183	11.57	138.038	99.94	1445.440	100.00
0.013	0.00	0.133	0.00	1.445	2.44	15.136	11.40	158.433	100.00	1660.537	100.00
0.015	0.00	0.156	0.00	1.660	3.05	17.318	11.60	181.970	100.00	1805.481	100.00
0.017	0.00	0.182	0.00	1.905	3.70	19.953	11.80	208.930	100.00	2157.762	100.00
0.020	0.00	0.206	0.00	2.188	4.35	22.006	11.73	238.893	100.00	2511.800	100.00
0.023	0.00	0.240	0.00	2.512	4.98	25.300	12.47	275.425	100.00	2884.032	100.00
0.026	0.00	0.275	0.00	2.884	5.55	30.200	14.50	316.235	100.00	3311.311	100.00
0.030	0.00	0.316	0.00	3.311	6.07	34.074	16.68	363.076	100.00	3601.894	100.00
0.035	0.00	0.363	0.00	3.602	6.54	39.811	25.88	416.689	100.00	4365.158	100.00
0.040	0.00	0.417	0.00	4.395	7.01	45.709	35.59	478.830	100.00	5011.672	100.00
0.046	0.00	0.479	0.00	5.012	7.50	52.481	47.85	549.541	100.00	5754.360	100.00
0.052	0.00	0.550	0.00	5.754	8.04	60.226	61.15	630.957	100.00	6606.834	100.00
0.060	0.00	0.631	0.19	6.607	8.67	69.103	73.85	724.436	100.00	7589.776	100.00
0.068	0.00	0.724	0.38	7.589	9.38	79.433	84.48	831.764	100.00	8709.608	100.00
0.078	0.00	0.832	0.66	8.710	10.08	91.201	92.19	954.993	100.00	10000.000	100.00
0.091	0.00	0.955	0.90	10.000	10.75	104.713	98.92	1093.478	100.00		

Figure 22(b)

Result Analysis Report

Particle Name: VR004	Accessory Name: Hydro 2000SM (A)	Obscuration: 15.83	%
Particle 3.000 Absorption: 0.05	Analysis model: General purpose	Obscuration (blue): 15.22	%
Dispersant: Cyclohexane	Dispersant RI: 1.426	Weighted Residual: 0.752	%
Vol. Weighted Mean D[4,3]: 2.587 μm	Mode: 2.468 μm	Specific Surface Area: 3.19	m^2/g
Surface Weighted Mean D[3,2]: 1.860 μm	Span: 1.539	Concentration: 0.0038	%Vol
Result units: Volume	Uniformity: 0.479		
d(0.1): 1.033 μm	d(0.5): 2.290 μm	D(0.60): 2.65 μm	d(0.9): 4.557 μm

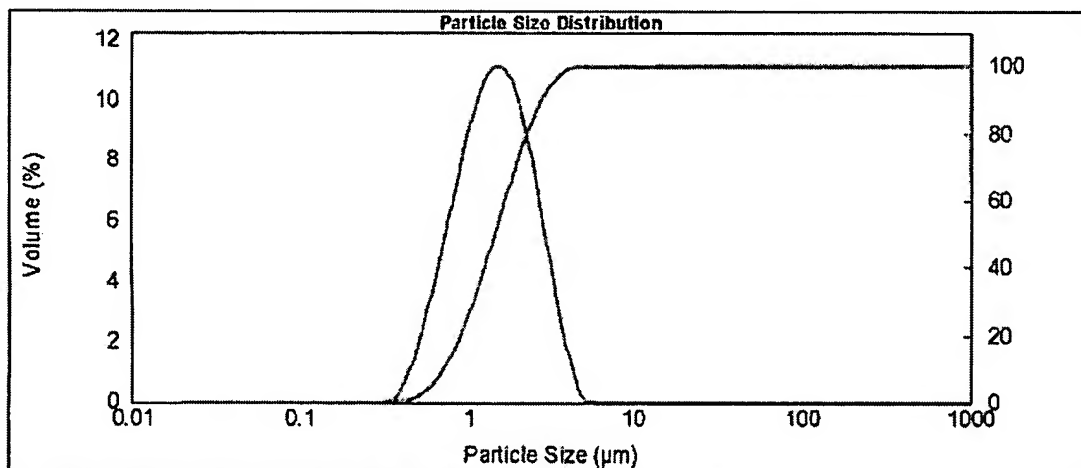


Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %
0.010	0.00	0.105	0.00	1.000	11.76	11.482	100.00	120.225	100.00	1258.928	100.00
0.011	0.00	0.120	0.00	1.250	16.61	13.103	100.00	138.038	100.00	1445.440	100.00
0.013	0.00	0.136	0.00	1.445	22.64	15.130	100.00	158.488	100.00	1658.527	100.00
0.015	0.00	0.156	0.00	1.660	29.69	17.378	100.00	181.570	100.00	1905.481	100.00
0.017	0.00	0.182	0.00	1.905	37.99	19.983	100.00	208.930	100.00	2187.762	100.00
0.020	0.00	0.209	0.00	2.188	48.96	22.909	100.00	239.863	100.00	2511.886	100.00
0.023	0.00	0.240	0.00	2.512	58.28	26.303	100.00	275.423	100.00	2894.032	100.00
0.028	0.00	0.275	0.00	2.884	68.57	30.200	100.00	316.228	100.00	3311.311	100.00
0.033	0.00	0.318	0.00	3.311	74.29	34.674	100.00	363.978	100.00	3601.894	100.00
0.036	0.00	0.363	0.00	3.802	82.00	39.911	100.00	418.889	100.00	4386.159	100.00
0.040	0.00	0.417	0.08	4.365	88.34	45.739	100.00	478.680	100.00	5011.872	100.00
0.046	0.00	0.479	0.33	5.012	93.15	52.461	100.00	543.541	100.00	5734.300	100.00
0.052	0.00	0.560	0.85	5.754	96.46	60.256	100.00	630.967	100.00	6606.934	100.00
0.060	0.00	0.621	1.73	6.607	98.48	69.183	100.00	724.436	100.00	7586.776	100.00
0.069	0.00	0.724	3.11	7.580	99.52	79.433	100.00	831.764	100.00	8700.636	100.00
0.076	0.00	0.832	5.18	8.710	99.92	91.201	100.00	954.683	100.00	10000.000	100.00
0.081	0.00	0.955	7.96	10.000	100.00	104.713	100.00	1095.478	100.00		

Figure 23(a)

Result Analysis Report

Particle Name: VR004	Accessory Name: Hydro 2000SM (A)	Obscuration: 10.59 %
Particle RI: 3.000 Absorption: 0.05	Analysis model: General purpose	Obscuration (blue): 12.66 %
Dispersant: Cyclohexane	Dispersant RI: 1.426	Weighted Residual: 0.774 %
Vol. Weighted Mean D[4,3]: 1.623 μm	Mode: 1.517 μm	Specific Surface Area: 4.75 m^2/g
Surface Weighted Mean D[3,2]: 1.283 μm	Span: 1.406	Concentration: 0.0016 %Vol
Result units: Volume	Uniformity: 0.436	
d(0.1): 0.727 μm	d(0.5): 1.453 μm	D(0.50): 1.67 μm
		d(0.9): 2.770 μm



VR004, Monday, November 25, 2002 2:01:06 PM

Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %
0.010	0.00	0.105	0.00	1.098	90.53	11.482	100.00	120.228	100.00	1258.805	100.00
0.011	0.00	0.110	0.00	1.219	98.77	13.183	100.00	136.038	100.00	1426.440	100.00
0.013	0.00	0.136	0.00	1.445	99.60	15.135	100.00	155.489	100.00	1659.587	100.00
0.015	0.00	0.156	0.00	1.600	99.87	17.378	100.00	181.970	100.00	1905.401	100.00
0.017	0.00	0.182	0.00	1.805	99.93	19.663	100.00	206.980	100.00	2187.752	100.00
0.020	0.00	0.208	0.00	2.108	99.16	22.908	100.00	239.883	100.00	2511.886	100.00
0.023	0.00	0.240	0.00	2.512	98.08	30.303	100.00	275.423	100.00	2884.032	100.00
0.025	0.00	0.275	0.00	2.884	91.54	30.300	100.00	315.228	100.00	3311.311	100.00
0.030	0.00	0.316	0.00	3.311	90.73	34.874	100.00	353.078	100.00	3801.894	100.00
0.035	0.00	0.363	0.00	3.802	99.32	39.811	100.00	415.688	100.00	4385.198	100.00
0.040	0.00	0.417	0.23	4.355	99.85	45.706	100.00	478.030	100.00	5011.672	100.00
0.045	0.00	0.479	1.10	5.012	99.97	52.481	100.00	549.541	100.00	5754.369	100.00
0.052	0.00	0.560	2.67	5.754	100.00	60.255	100.00	630.957	100.00	6606.934	100.00
0.060	0.00	0.631	5.74	6.607	100.00	69.183	100.00	724.439	100.00	7505.779	100.00
0.069	0.00	0.724	9.88	7.586	100.00	79.433	100.00	831.764	100.00	8702.536	100.00
0.079	0.00	0.832	15.46	8.710	100.00	91.201	100.00	954.953	100.00	10000.000	100.00
0.091	0.00	0.955	22.37	10.000	100.00	104.713	100.00	1098.478	100.00		

Operator notes: Lebbbook 273-053

Figure 23(b)

Figure 24

Stability Condition	Formulation	Assay - Initial	Rel subs (highest Indiv peak%) - Initial	Rel subs (sum of rel peaks)-Initial
Initial	Batch1	ND	0.03	0.7
	Batch2	ND	0.04	0.10
	Batch3	101	0.03	0.07
	Batch4	101	0.04	0.09
25 °C/60% RH	Formulation	Assay - 1 month	Rel subs (highest Indiv peak%) - 1 month	Rel subs (sum of rel peaks) - month
	Batch1	99	0.04	0.10
	Batch2	99	0.06	0.20
	Batch3	99	0.05	0.20
40 °C/75% RH	Batch4	98	0.05	0.14
	Formulation	Assay - 1 month	Rel subs (highest Indiv peak%) - 1 month	Rel subs (sum of rel peaks) - month
	Batch1	98	0.04	0.14
	Batch2	100	0.08	0.20
	Batch3	99	0.04	0.14
	Batch4	98	0.13	0.28

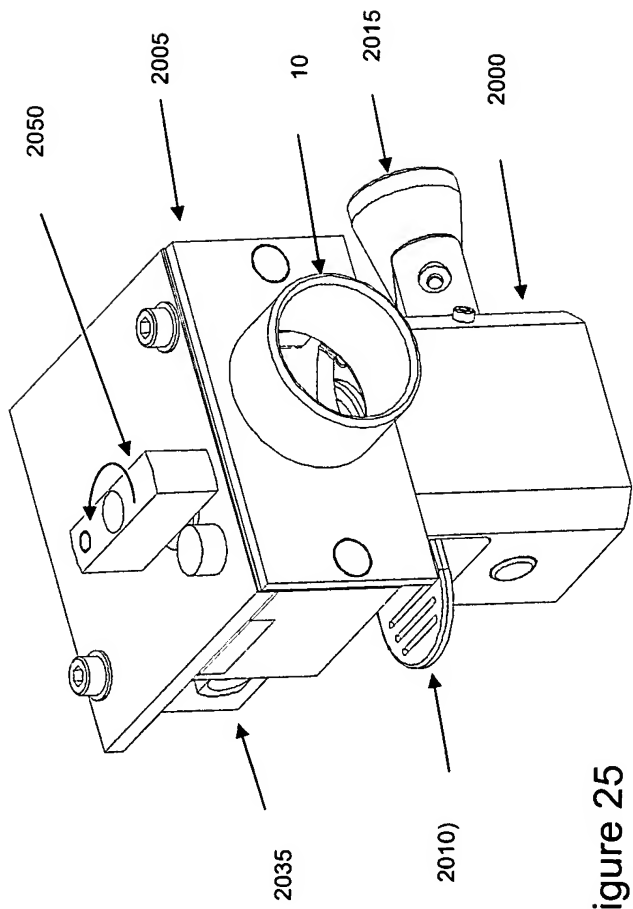


Figure 25

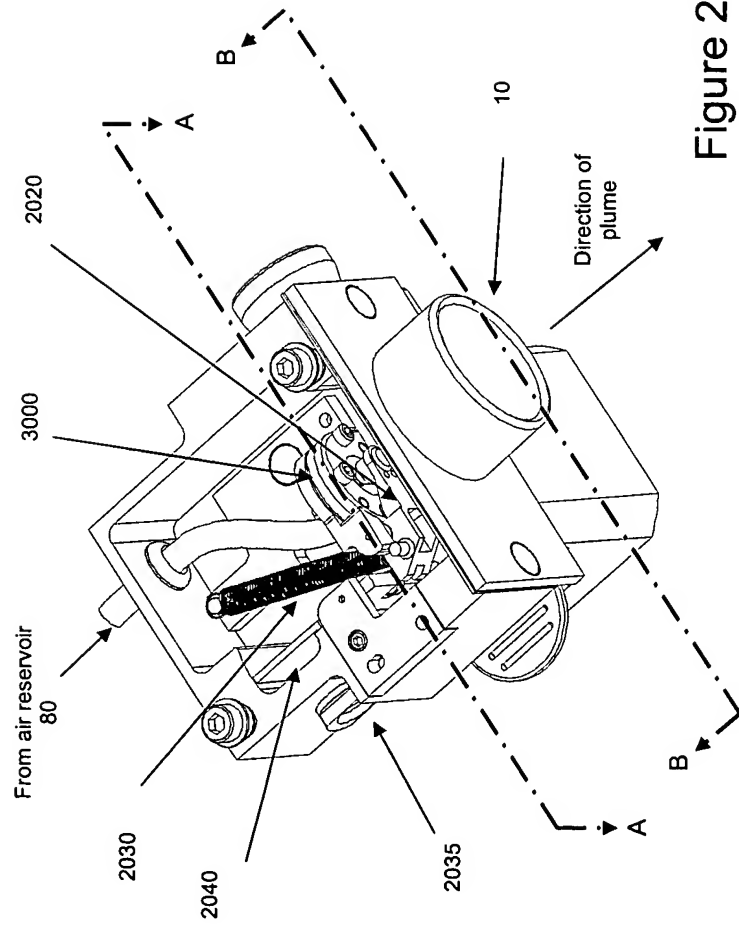


Figure 26

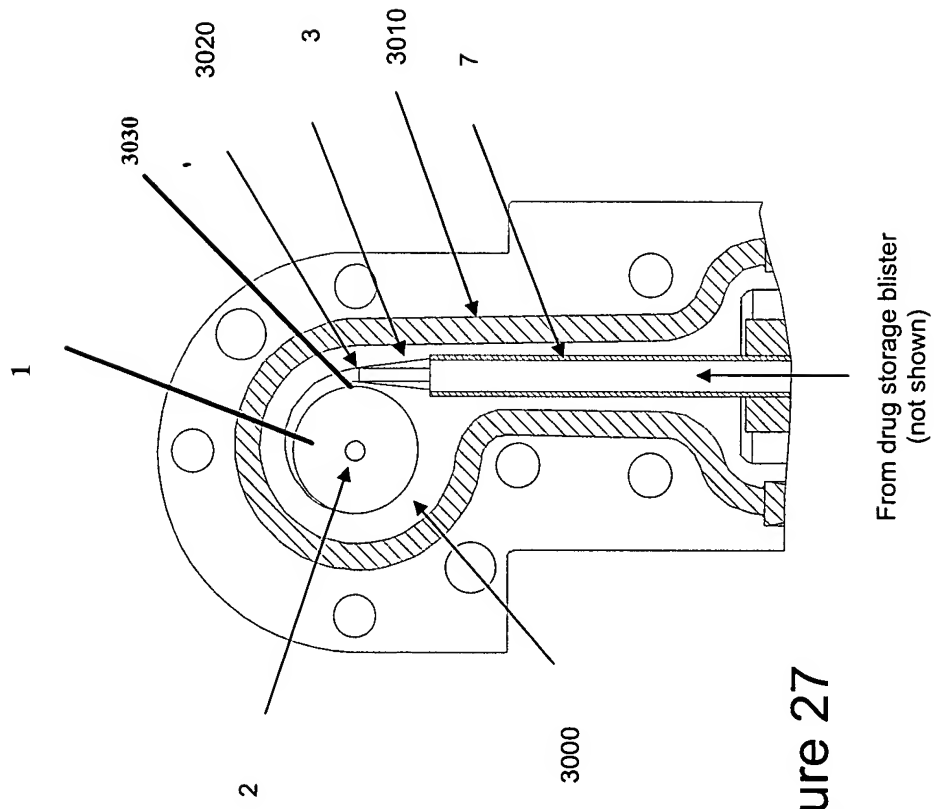


Figure 27

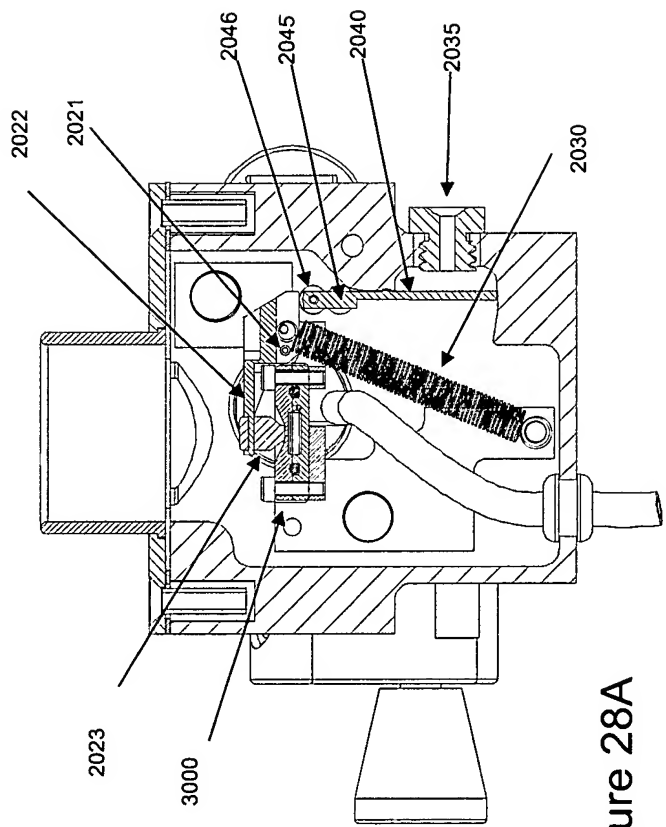


Figure 28A

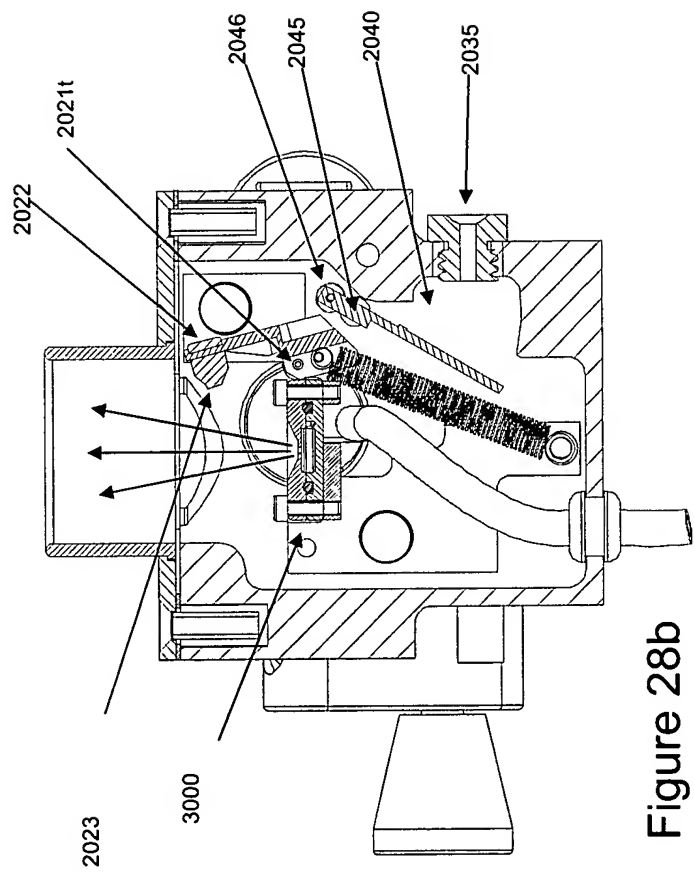


Figure 28b

Figure 29A

Formulation Details 5000	Uniformity of Delivered Dose 6000 (DUSA, n=10)						Fine Particle Performance (<5 µm Cut-Off) 7000 MSLI (ACI)							
	Drug Retention 6010		6015 DD (µg)	6020 Metered (µg)	6025 Mass Balance (%)	7005 n=	Drug Retention 7010		7015 DD (µg)	7020 FPD (µg)	7025 FPF (%)	7030 Metered	7035 Mass Balance (%)	7036 Test Flow Rate (L min ⁻¹)
	Blister (µg) 6012	Device (µg) 6013						Blister (µg) 6012	Device (µg) 6013					
100 µg 45 - 63 µm Inversina	7.2	4.3	84	95	93	3 (1)	7.7 (7.5)	7.5 (7.2)	85 (76)	56 (52)	66 (68)	100 (91)	95 (88)	95 (95)
100 µg 5 - 63 µm Air Jet Inversina	7.3	3.6	85	95	92	3	4.4	5.7	82	55	66	92	89	95
100 µg 45-63 µm Grindomix	Not Done					3	6.9	8.6	78	39	50	93	94	95
100 µg 30 - 63 µm Air Jet Grindomix	Not Done					3	5.4	6.3	86	40	47	97	96	95
100 µg 45 - 63 µm Air Jet Grindomix	Not Done					3	4.2	9.4	83	52	62	97	92	95
200 µg UF020100MGA 45 - 63 µm Air Jet Inversina	10.0	5.3	188	203	96	(2)	(7.8)	(14.5)	(175)	(122)	(70)	(197)	(94)	60

Figure 29B

Formulation Details 5000	Uniformity of Delivered Dose 6000 (DUSA, n=11)						Fine Particle Performance (<5 µm Cut-Off) 7000 MSL(n=2)					
	Drug Retention 6010		Delivered Dose 6015		Metered Dose 6020		Mass Balance 6025		Drug Retention 7010		Delivered Dose µg 7015	
	Blister (µg) 6012	Device (µg) 6013	(µg) 6016	% nominal 6017	(µg) 6020	(µg) 6025	(µg) 6012	Device (µg) 7013	Blister (µg) 6012	Device (µg) 7013	µg 7015	FPD (µg) 7020
100 µg 45 - 63 µm Inversina	6.6	7.8	81	81	95	95	8.8	5.6	82	52	64	7030
200 µg 45 - 63 µm t Inversina	12.1	11.5	170	85	194	93	9.8	13.3	175	118	67	198
200 µg 45-63 µm Inversina	9.2 14.5	12.7 8.6	162 169	81 85	184 192	93 96	6.5	15.2	170	105	62	192
200 µg 45 - 63 µm Inversina	11.0	11.2	171	85	193	95	10.7	14.1	172	117	68	196

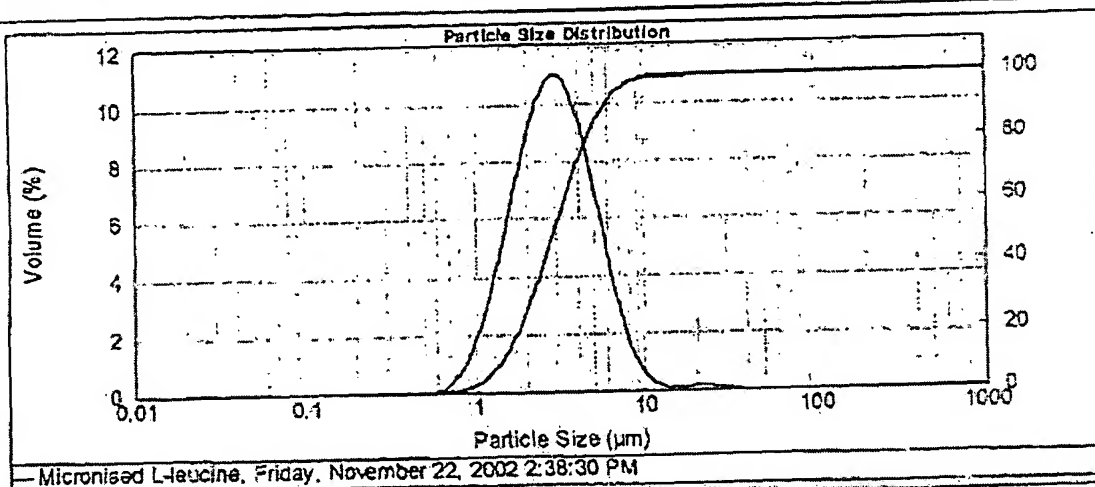
Test Flow Rate = 60 L Min⁻¹

Sample Name:
Micronised L-leucine

Sample Source:
Micromacinazione

Sample batch number:
MM0001

Particle Name: Leucine	Accessory Name: Hydro 2000SM (A)	Obscuration:	7.95	%
Particle 1.345 Absorption: 1.5	Analysis model: General purpose	Obscuration (blue):	9.23	%
Dispersant: Cyclohexane	Dispersant RI: 1.428	Weighted Residual:	0.422	%
Vol. Weighted Mean D[4,3]:	3.405 μm	Mode: 2.953 μm	Specific Surface Area:	2.33 m^2/g
Surface Weighted Mean D[3,2]:	2.521 μm	Span: 1.487	Concentration:	0.0025 %Vol
Result units: Volume	Uniformity: 0.494			
d(0.1): 1.442 μm	d(0.5): 2.905 μm	D(0.60): 3.34 μm	d(0.9): 5.765 μm	



Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %	Size (μm)	Vol Under %
0.010	0.00	0.105	0.00	1.095	3.33	11.482	99.23	120.226	100.00	1258.925	100.00
0.011	0.00	0.120	0.00	1.259	6.09	13.183	99.38	138.038	100.00	1445.440	100.00
0.013	0.00	0.138	0.00	1.445	10.07	15.136	99.46	158.489	100.00	1659.587	100.00
0.015	0.00	0.158	0.00	1.660	15.46	17.378	99.54	181.970	100.00	1905.461	100.00
0.017	0.00	0.182	0.00	1.905	22.25	19.953	99.64	208.930	100.00	2187.762	100.00
0.020	0.00	0.209	0.00	2.188	30.41	22.909	99.76	239.883	100.00	2511.886	100.00
0.023	0.00	0.240	0.00	2.512	39.62	26.303	99.87	275.423	100.00	2884.032	100.00
0.026	0.00	0.275	0.00	2.884	49.45	30.200	99.96	316.228	100.00	3311.311	100.00
0.030	0.00	0.316	0.00	3.311	59.38	34.674	100.00	363.078	100.00	3801.894	100.00
0.035	0.00	0.363	0.00	3.802	68.85	39.811	100.00	416.869	100.00	4365.158	100.00
0.040	0.00	0.417	0.00	4.365	77.31	45.709	100.00	478.630	100.00	5011.872	100.00
0.046	0.00	0.479	0.00	5.012	84.41	52.481	100.00	549.541	100.00	5754.399	100.00
0.052	0.00	0.550	0.00	5.754	89.94	60.256	100.00	630.957	100.00	6606.934	100.00
0.060	0.00	0.631	0.00	6.607	93.92	69.183	100.00	724.436	100.00	7585.776	100.00
0.069	0.00	0.724	0.12	7.586	96.53	79.433	100.00	831.764	100.00	8709.636	100.00
0.079	0.00	0.832	0.61	8.710	98.07	91.201	100.00	954.983	100.00	10000.000	100.00
0.091	0.00	0.955	1.59	10.000	98.88	104.713	100.00	1096.478	100.00		

Figure 30

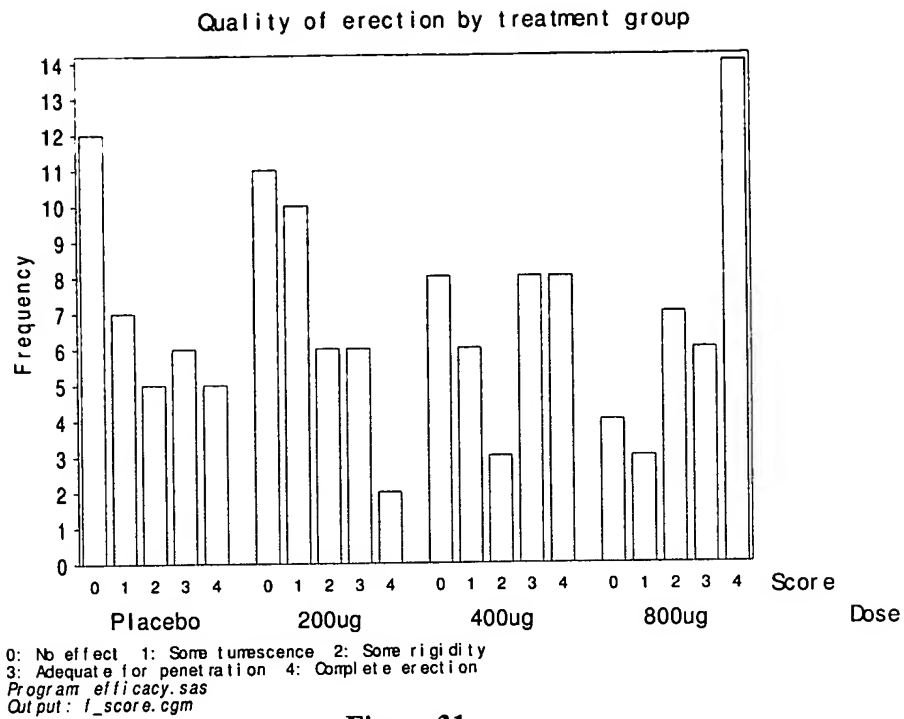


Figure 31

Response Rate by Treatment Group

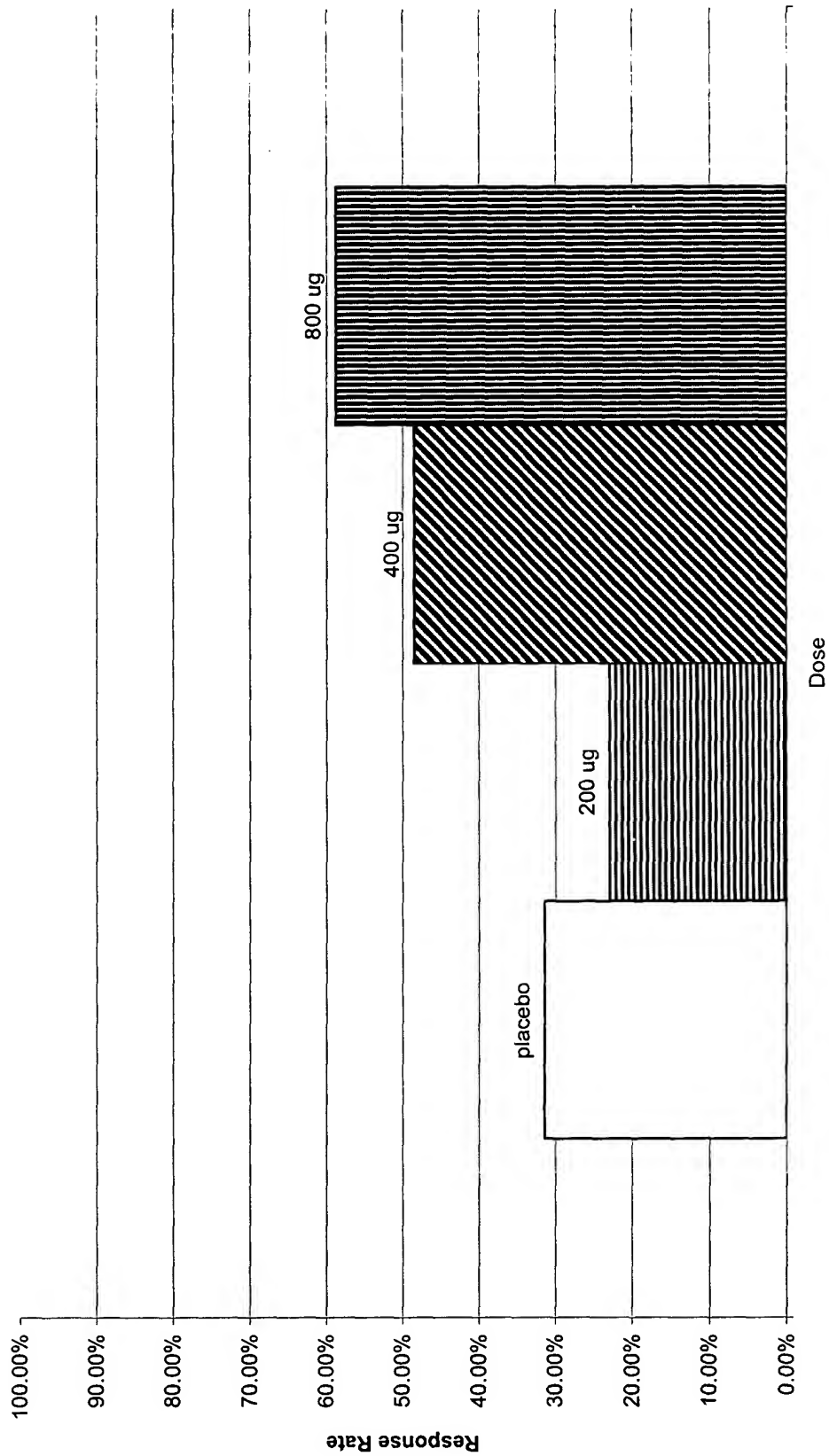


Figure 32

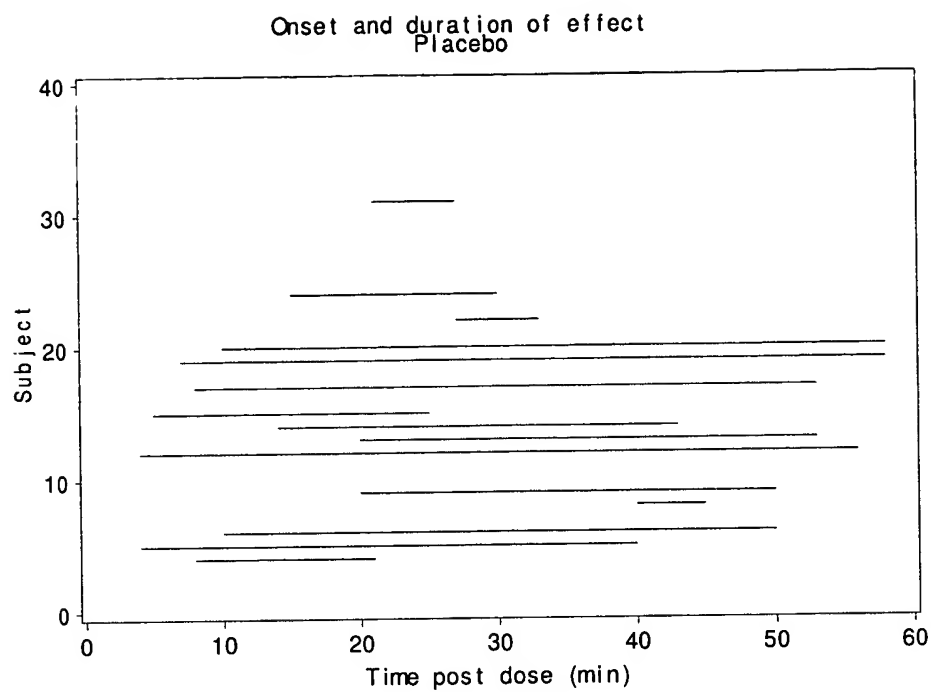


Figure 33

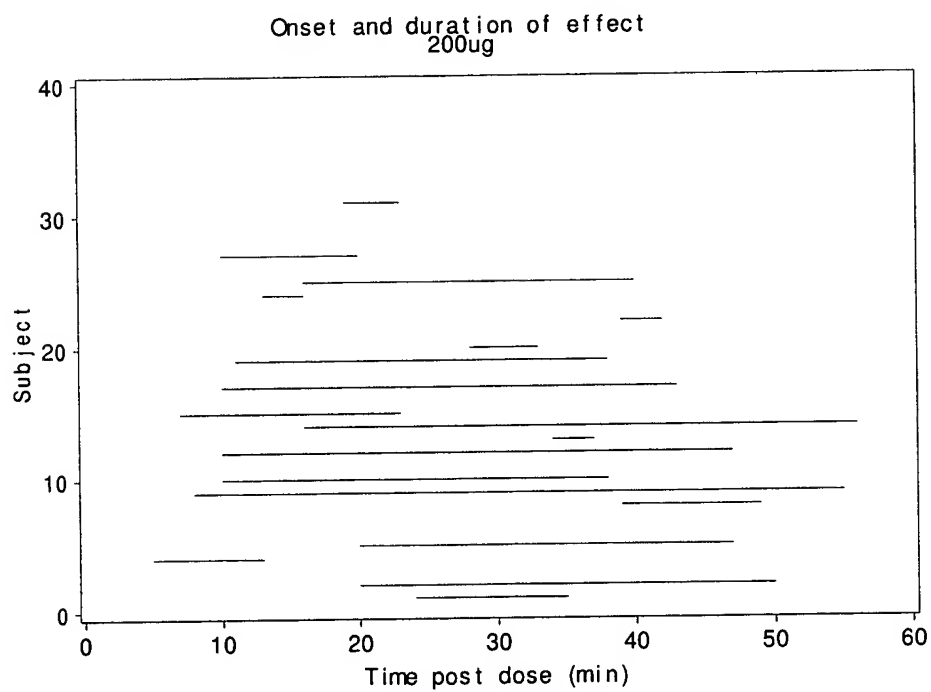


Figure 34

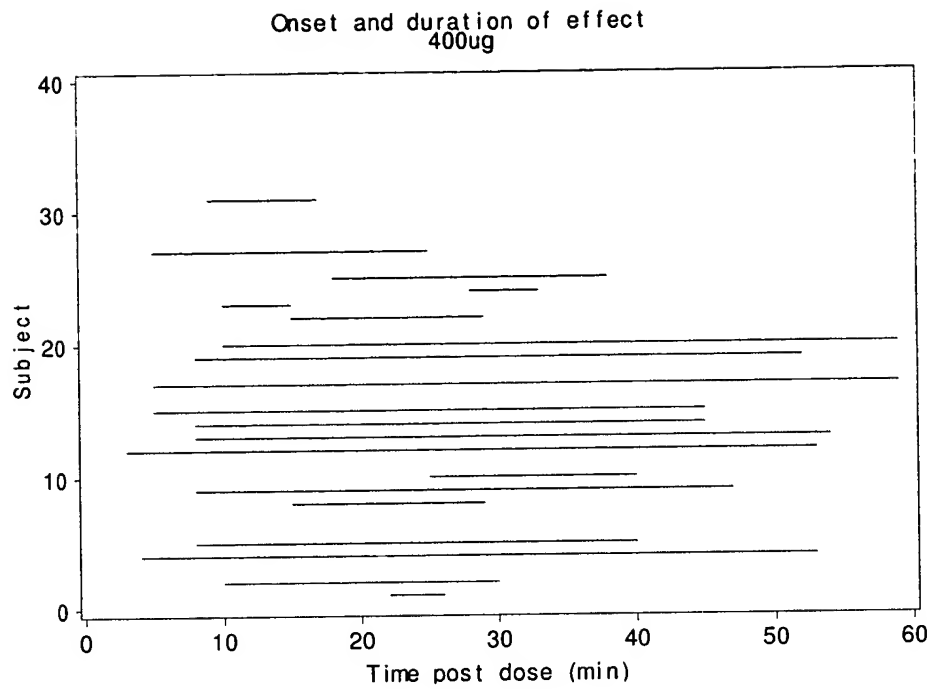


Figure 35

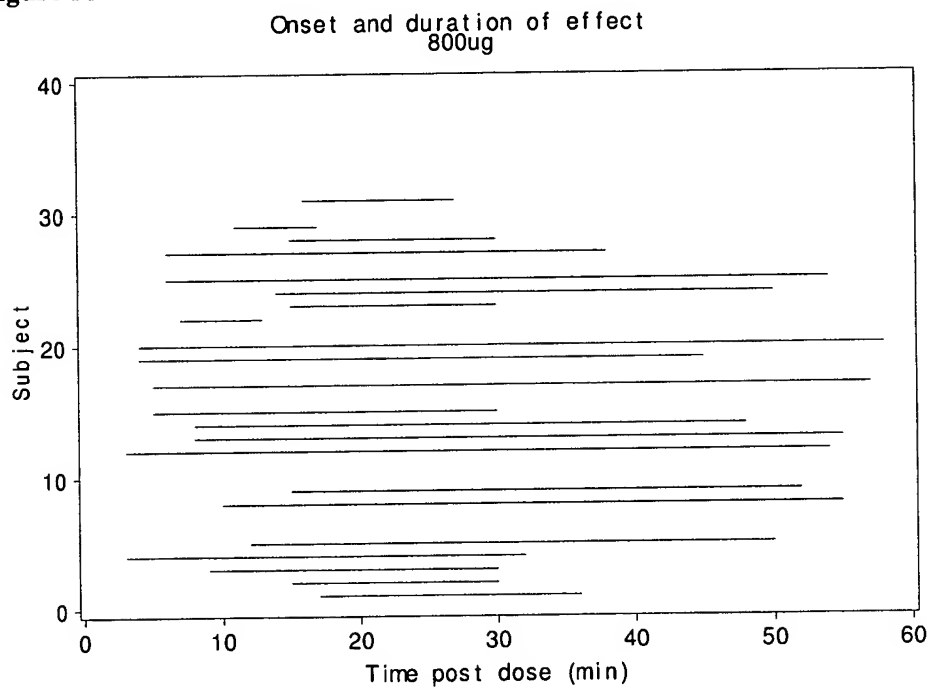


Figure 36

Figure 37

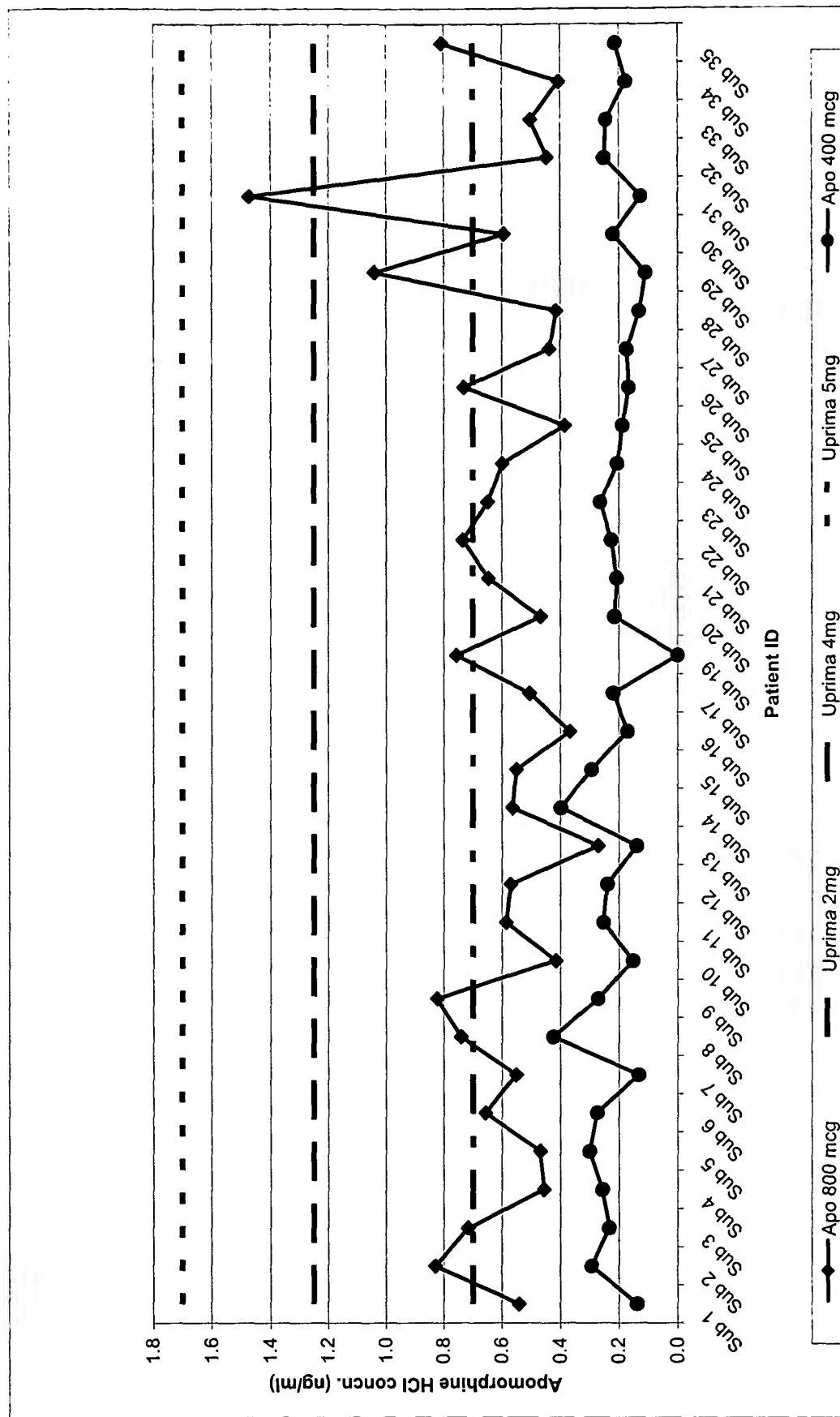
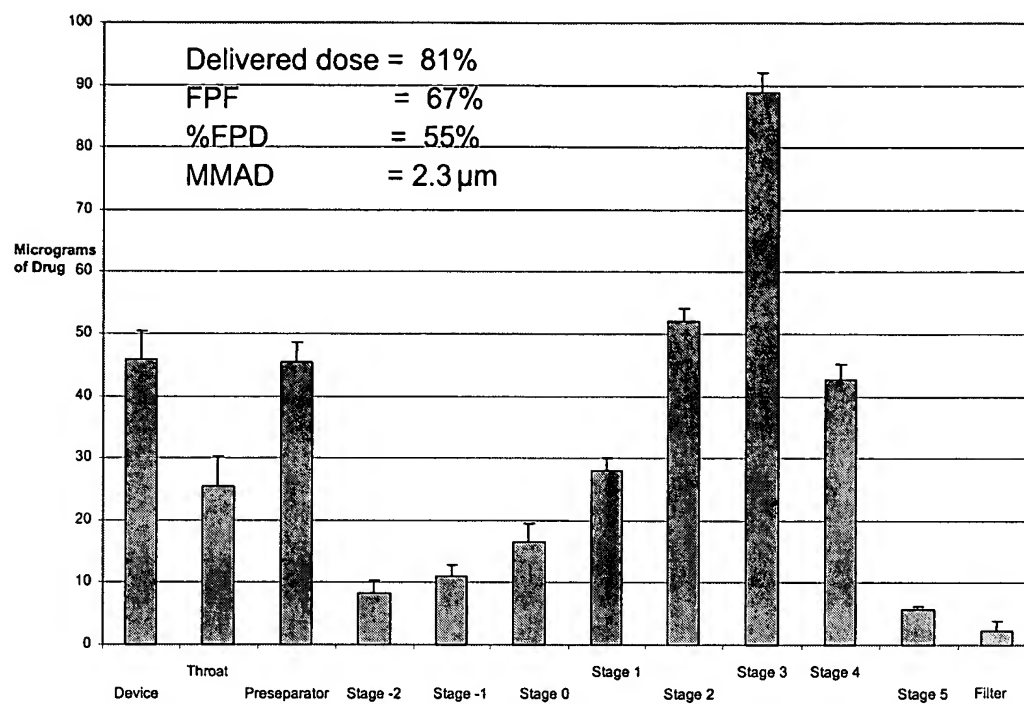


Figure 38



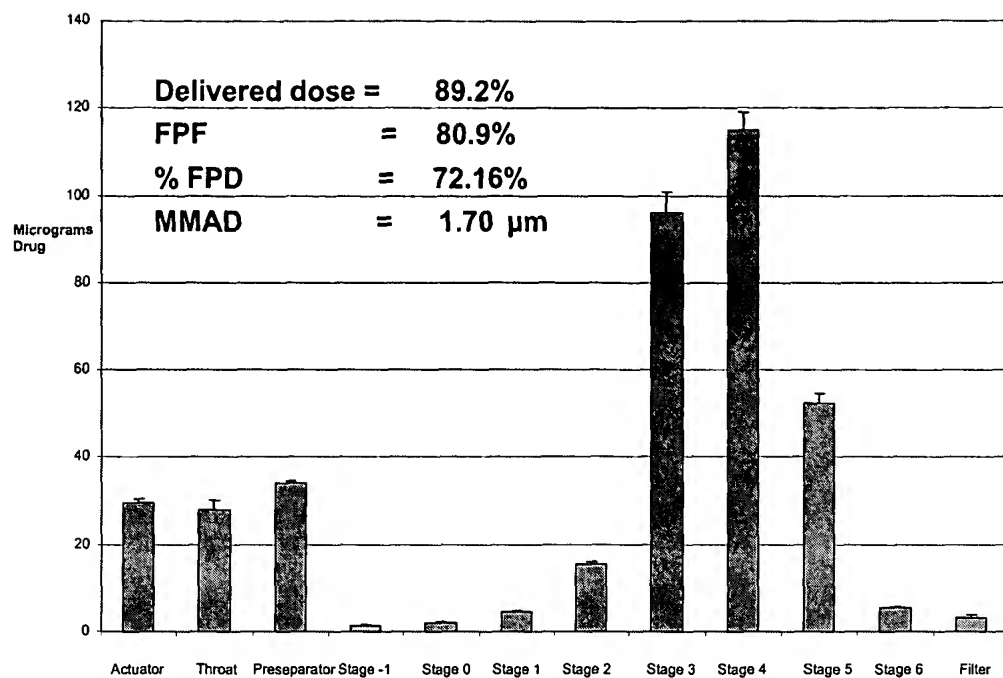


Figure 39